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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,541	04/26/2002	Larry A. Wheeler	17400(BAR)	1687

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,541	WHEELER ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/02;2/02;3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 10/18/04. The amendment has been entered. Claims 16-22 and 30 are currently pending in the application and are addresses herein.

Election/Restrictions

Applicant's election without traverse of Group XI in the reply filed on 10/18/04 is acknowledged. It is also acknowledged that claims 17 and 30 read directly on the elected invention, and that amended claims 21 and 22 are now joined with the claims of the elected invention as they have been amended to depend on claim 16. It is pointed out that claims 1-15, 23-29 and 31-38 have been cancelled. Claims 16-22 and 30 are examined herein.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Specifically, see page 6, line 11; page 7, line 27; and page 8, line 25. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Additionally, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence

Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. Specifically, see page 4, lines 18-26; page 6, lines 4-7; page 7, lines 20-23; and page 8, lines 14-21. It is noted that Applicants have submitted a Paper sequence listing and CRF, which appear to contain the disclosed sequences. However, the disclosed sequences have not been assigned appropriate sequence identifiers (i.e., SEQ ID Nos.). It is noted that amending the specification such that the sequences are disclosed in the proper format and given the appropriate sequence identifier would obviate this objection. If the paper sequence listing does not contain the disclosed sequences, then a proper substitute sequence listing and CRF is required.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 1/4/02, 2/12/02, and 3/28/03 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objections

Claim 17 is objected to for encompassing non-elected subject matter. As indicated in the communication filed 10/18/04, applicants have elected, without traverse, a method for preventing cell death induced by PDT wherein the method comprises administering brimonidine. Claim 17 includes the non-elected subject matter: NGF, PEDF, CNTF, BDNF and memantine (Groups VII-X and XII, respectively). Applicants are required to cancel the non-elected subject matter.

Claim 30 recites, "an therapeutically effective amount of a angiogenic compound" (see line 2). It appears that applicants have made a typographical error referring to "an therapeutically effective amount" and "a angiogenic compound", thus rendering the claim grammatically incorrect. It is noted that amending the claim to "a therapeutically effective amount" and "an angiogenic compound" would obviate this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 18 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the limitation "said PDT treatment" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 30 recites the limitation "said composition" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

It is noted that claim 16 is the independent claim from which claims 18 and 30 depend. As such, claim 16 is also indefinite, as the independent claim must encompass all limitations of claims which depend therefrom.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof.

The instant claims are drawn to a method of protecting ocular neural tissue from damage caused by photodynamic therapy (PDT) comprising delivering to a patients ocular neural tissue an amount of a neuroprotectant compound effective to protect a plurality of ocular neurons from cell death as compared to ocular neuron cell death observed in the absence of the administration of said neuroprotectant (e.g., see claim 1) and wherein the composition also comprises an

therapeutically effective amount of an antioangiogenic compound (e.g., see claim 30). Therefore, the claims encompass a genus of neuroprotectant compounds and antiangiogenic compounds wherein each genus comprises a undefined number of species molecules, however, given the broadest reasonable interpretation, each genus can encompass thousands of different molecules, including molecules that are recognized in the art as having substantial structural and functional variation. For instance, each genus encompasses peptide molecules, polypeptide molecules, antibody molecules, polynucleotide molecules encoding functional polypeptides, antisense nucleic acid molecules, organic and inorganic compounds including small molecule compounds, etc. It is noted that polypeptides are comprised of amino acids, polynucleotides are comprised of nucleic acids, and small molecules can be organic or inorganic compounds unrelated to nucleic acids or amino acids. With respect to the specific function molecules encompassed by the claims, it is noted that neuroprotectant and antiangiogenic compounds can exert their effect through different biochemical pathways, including targeting different specific molecules. As such, each claimed genus, given the broadest reasonable interpretation, can encompasses thousands of different molecules wherein the molecules can have substantial structural and functional variation.

It is acknowledged that the specification has disclosed six specific different neuroprotectant compounds: NGF, PEDG, CNTF, BDNF, brimonidine and memantine, which are recognized in the prior art (as acknowledged in the specification). Additionally the specification discloses that PEDF is also an anti-angiogenic molecule (e.g., see p. 3, second full paragraph), and PEDF is the only antiangiogenic compound disclosed in the specification. It is noted that the specification does not disclose any structural elements that are shared by all

species of neuroprotectant and antiangiogenic molecules and which are critical to the function of the molecules. As such, applicants have not indicated any structure-function relationship for each genus of claimed molecules. Since the claims are drawn to neuroprotectant and antiangiogenic molecules that encompass molecules that are recognized as having substantial structural and functional variation, and further considering that the specification has not disclosed any structure-function relationship for each of the claimed genus of molecules, the specification has not adequately described a the genus of neuroprotectant molecules nor the genus of antiangiogenic molecules encompassed by the claims.

Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of protecting ocular neural tissue from damage caused by photodynamic therapy (PDT) comprising delivering to a patient's ocular neural tissue an amount of a neuroprotectant compound effective to protect a plurality of ocular neurons from cell death as compared to ocular neuron cell death observed in the absence of the administration of said neuroprotectant, wherein said neuroprotectant is brimonidine does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

As mentioned above, the claims encompass a method comprising administration of neuroprotectant and antiangiogenic compounds wherein the neuroprotectant and antiangiogenic compounds can be any of a vast number of different species. As indicated above, the compounds encompassed by the claims include molecules that are recognized as having substantial structural and functional variation. Furthermore, the specification has only disclosed 6 specific neuroprotectant compounds one of which is also the only disclosed antiangiogenic compound. Therefore, the specification has not described a representative number of species encompassed by the claims. Without a clear and adequate description of a representative number of compounds encompassed by the claims, one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation to identify a representative number of claimed compounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.).

Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature and includes enhancing the PDT method by administering an antiangiogenic compound and a neuroprotectant compound that represses apoptosis in cells or tissues surrounding the treatment (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted the specification of the instant application acknowledges that PDT (which is recognized as requiring the use of a photosensitizing agent) can damage optical neural tissue. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). Regarding the anti-apoptotic compound, Miller teaches that the anti-apoptotic compound is useful for decrease a cell's sensitivity to PDT, and specifically indicates that BDNF, PEDF are two anti-apoptotic compounds that can be used in the method (it is noted that the instant specification also discloses BDNF and PEDF as neuroprotective compounds). Miller also teaches that the anti-apoptotic compound can be administered sufficiently before the PDT treatment to allow the compound to localize to the site of treatment (e.g., see claims 20, 23; paragraphs 17-19 and 70, especially paragraph 17). Furthermore, Miller teaches that the anti-apoptotic neuroprotecant compound can be delivered by any mode of administration (e.g., see paragraph 66), and specifically teaches intravenous administration, intravitreal administration,

intraocular administration and delivery to the inner wall of the eye (which would necessarily be a subretinal delivery) (e.g., see paragraphs 69-70, especially paragraph 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.) in view of Wheeler et al. (Europ. Jour. Ophthal., JAN-MAR 1999).

As indicated above, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound and a neuroprotectant compound that represses apoptosis in cells or tissues surrounding the treatment (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted the specification of the instant application acknowledges that PDT (which is recognized as requiring the use of a photosensitizing agent) can damage optical neural tissue. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). Regarding the anti-apoptotic

compound, Miller teaches that the anti-apoptotic compound is useful for decrease a cell's sensitivity to PDT, and specifically indicates that BDNF, PEDF are two anti-apoptotic compounds that can be used in the method (it is noted that the instant specification also discloses BDNF and PEDF as neuroprotective compounds).

Miller does not teach that the neuroprotectant compound is Brimonidine.

However, Wheeler teaches that Brimonidine is an alpha-2 agonist compound that is neuroprotective in animal models of retinal and optic nerve injury (e.g., see title, abstract, etc.).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to perform the method taught by Miller and substitute Brimonidine as the neuroprotective agent with a reasonable expectation of success because Wheeler teaches that Brimonidine is a neuroprotective agent.

One of ordinary skill in the art would have been motivated to substitute Brimonidine as the neuroprotective agent in Miller's method because Wheeler teaches that Brimonidine is an anti-apoptotic neuroprotective agent that can be used to protect target cells from neuronal injury (e.g., see p. S21, first column).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16- 22 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,856,329 (hereafter '329) in view of Miller et al (US 2002/0040015 A1).

The '329 patent teaches that Brimonidine is neuroprotective agent that can be used to protect an optic nerve from damage caused by a noxious action, (e.g., see claims, especially claims 1 and 12).

The '329 patent does not teach that the noxious action is photodynamic therapy.

However, as indicated above, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound and a neuroprotectant compound that represses apoptosis in cells or tissues surrounding the treatment (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted the specification of the instant application acknowledges that PDT (which is recognized as requiring the use of a photosensitizing agent) can damage optical neural tissue. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). Regarding the anti-apoptotic compound, Miller teaches that the anti-apoptotic compound is useful for decrease a cell's

sensitivity to PDT, and specifically indicates that BDNF, PEDF are two anti-apoptotic compounds that can be used in the method (it is noted that the instant specification also discloses BDNF and PEDF as neuroprotective compounds).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to use the method taught by the '329 patent (using Brominidine as a neuroprotectant) to protect ocular tissue from the noxious effects of PDT, with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to use the method to protect ocular tissue from PDTR damage because the '329 patent is disclosed as a method of protecting ocular tissue from damage caused by a any noxious agent and the prior art recognizes that PDT can cause damage to ocular tissue.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell
Art unit 1635

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PRIMARY EXAMINER